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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
MORAN, MARJORIE A

ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/942,369	Applicant(s) CHEN ET AL.	
	Examiner Marjorie Moran	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-24,26 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-24,26 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. All rejections and objections not repeated below are hereby withdrawn.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/7/02 has been entered. Claims 20-24, 26, and 31 are pending.

Response to Arguments

The declaration and arguments filed 1/7/02 have been fully considered but are not persuasive for the following reasons:

In response to applicant's arguments in the response and declaration filed 1/7/02 that the MacConkey agar of LIBMAN is not a uropathogenic specific medium because it fails to allow for growth of primary gram negative urinary pathogens, it is noted that there is no evidence to support this statement. It appears from the statement of the declaration that the conclusion for lack of growth is based on lack of detection of a signal from a single fluorogenic substrate in MacConkey agar. As supported by the teachings of CARR *et al.* (US 5,064,756, col. 4, lines 53-56), it is known that poor fluorescence can result for a variety of reasons, even in the presence of growing microorganisms. It is also known in the art that some combinations of medium or sample and fluorophores can result in poor fluorescence (i.e. the signal can be "damped" by the composition of the medium and/or sample). Thus, it is unclear whether

MacConkey agar did not support growth of microorganisms, as alleged by applicants, or whether microorganismal growth occurred, but the fluorescent signal generated was weak/inhibited such that the growth was not detected. The fact that growth was detected in some samples indicates that microorganismal growth is supported, but was not detected in some samples. The CHEN declaration does not provide evidence that MacConkey medium is not a uropathogenic specific medium (i.e. one which allows for growth of primary gram negative organisms responsible for 85-90% of urinary tract infections), only that the combination of MacConkey agar and MUP does not "work" as well as the medium disclosed in the instant specification for performing the claimed method. It is noted that evidence for unexpected results must be shown for elements of the *claimed* invention. The composition of the medium used for comparison to MacConkey agar in the CHEN declaration of 1/7/02 is not recited in the claims. The medium claimed is a uropathogenic specific medium, which is defined functionally in the specification. MacConkey agar, as taught by LIBMAN, meets the functional definition, as previously set forth and maintained. The evidence of the declaration, that MacConkey agar can be used for at least some samples to detect urinary pathogens and determine antibiotic susceptibility, indicates that MacConkey agar is a uropathogenic specific medium. It is noted that while the declaration states that MacConkey agar gave some "false negative" results, there is no indication that MacConkey agar gave "false positive" results (i.e. indicated growth of uropathogens in samples with non-urinary pathogenic organisms or no microorganisms), therefore the results of the declaration support the specificity of MacConkey agar for uropathogenic growth and detection. Applicant should note that the rejections set forth below do not recite MacConkey agar. The medium recited in the rejections herein is one comprising signal generating substrates and which allows for selective, differential detection of common gram-negative uropathogens.

Claim Rejections - 35 USC § 103

Claims 20-24 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over JOHNSON (US 4,077,845) in view of LIBMAN *et al.* (US 4,046,138) and THALLER *et al.* (J. Clinical Microbiol. (4/1988), vol. 26 (4), pp. 791-793).

Applicant's arguments with respect to claims 20-24 and the CHEN declaration filed 1/7/02 have been fully considered but are moot in view of the new ground(s) of rejection.

Claim 20 recites a method to simultaneously detect and determine the susceptibility of urinary pathogens to antimicrobial agents comprising (a) providing a multicompartment assay device with at least one compartment comprising a growth medium (capable of sustaining growth of total microbial organisms), at least one compartment comprising a uropathogenic specific medium (UTI medium) and at least one compartment comprising an antimicrobial susceptibility interpretation medium comprising an antimicrobial agent (interpretation medium), (b) placing a portion of the sample in each type of compartment, whereby metabolism of a signal generating substrate and production of a signal in the growth medium compartment indicates the presence of total microbial organisms, metabolism of a substrate and production of a signal in the UTI medium indicates the presence of uropathogens, and metabolism of a substrate and detection of a signal in the interpretation medium indicates that the organisms lack susceptibility to the antimicrobial agent in the interpretation medium, and (c) examining the compartments to determine the presence of uropathogens in the samples and susceptibility thereof to antimicrobial agents. Claim 21 limits the sample to urine. Claim 22 limits the organisms detected to primary gram negative urinary pathogens. Claim 23 limits the pathogens of claim 22 to Enterobacteriacae. Claim 24 limits the pathogens of claim 22 to be selected from E. coli, Klebsiella spp., Enterobacter spp., Proteus mirabilis, Proteus vulgaris, Morganella

morganii, Providencia retteri, and Acinobacter spp. Claim 31 limits the signal generating substrate of the method to be fluorogenic or chromogenic.

JOHNSON teaches a process (method) for detecting and determining the susceptibility of specific microorganisms to antibiotics wherein a clinical (urine) sample is added to separate wells of a microtiter plate, which wells comprise a selective culture medium or blends of the selective culture medium and known antibiotics, the plate is cultured, then the wells examined for growth of microorganisms (col. 10, line 45-col. 12, line 2 and col. 7, lines 33-36). JOHNSON further teaches that his method and device may be used to analyze urinary pathogens, specifically *Escherichia coli*, *Klebsiella*, *Enterobacter*, and *Proteus* spp. (col. 3, lines 31-36). JOHNSON teaches that his sample may be urine, blood or spinal fluid, and that growth in individual growth wells permits a positive test for indication of organisms (col. 7, lines 39-46). JOHNSON does not specifically teach a medium capable of sustaining growth of total microbial organisms nor a medium comprising a fluorogenic or chromogenic substrate.

LIBMAN teaches a device and method for detecting contaminating microorganisms (pathogens) in a urine sample wherein the sample is cultured on two or more different media, selective and nonselective (col. 3, lines 64-67). LIBMAN teaches that his nonselective media supports growth of urinary pathogens and contaminants.

THALLER teaches a selective, differential medium to screen for common gram-negative urinary tract pathogens (abstract), wherein the medium is inhibitory to growth of gram-positive organisms (p. 792, right column). THALLER teaches that metabolism of chromogenic and/or fluorogenic substrates in her medium can produce detectable signals whereby urinary pathogens are detected (p. 792, left column and Table 1). THALLER specifically teaches that microorganisms detected using her medium include E. coli, Klebsiella species, an Enterobacter species, Proteus species, Morganella, and Providencia (Table 1). THALLER teaches that her

medium provides several improvements over other selective media used in methods of detecting urinary pathogens (p. 792, right column).

It would have been obvious to one of ordinary skill in the art at the time of invention to include the nonselective medium of LIBMAN in the method of JOHNSON where the motivation would have been to provide a positive control for microorganismal growth, as suggested by JOHNSON. It would also have been obvious to use the selective medium of THALLER as the selective medium in the method of JOHNSON where the motivation would have been to "analyze very selectively" for organisms causing an infection (JOHNSON, col. 3, lines 31-35) in order to presumptively identify the causative organisms in order to determine an appropriate course of treatment, as suggested by both LIBMAN (col. 2, lines 48-53) and JOHNSON (col. 3, lines 30-39). One would also have been motivated to use the selective medium of THALLER in the method of JOHNSON and LIBMAN because it is an improvement over other selective medium such as that taught by LIBMAN. One skilled in the art would reasonably have expected success in incorporating the selective and nonselective media of THALLER and LIBMAN in the method of JOHNSON because JOHNSON teaches sustenance of growth of total microbial organisms, which implies use of a nonselective medium, and because JOHNSON specifically teaches use of selective media. One skilled in the art would also have reasonably expected success in using the T-mod medium of THALLER as a selective medium in the method of JOHNSON because the THALLER specifically teaches that her medium is a selective, differential medium which may be used to successfully detect and identify gram-negative microorganisms in urine samples (p. 791).

Claim 26 is newly rejected under 35 U.S.C. 103(a) as being unpatentable over JOHNSON (F) in view of LIBMAN *et al.* (H) and THALLER *et al.* (J. Clinical Microbiol. (4/1988), vol. 26 (4), pp. 791-793) as applied to claim 20 above, and further in view of BROCCO (E).

Applicant's arguments with respect to claim 26 have been considered but are moot in view of the new ground(s) of rejection.

Applicant claims a method of simultaneously detecting urinary pathogens in a biological sample and determining susceptibility of the pathogens to antimicrobial agents, as set forth above. Applicant further limits the antimicrobial agents to amoxicillin, clavulanic acid/amoxicillin, or enrofloxacin.

JOHNSON in view of LIBMAN and THALLER make obvious a method of simultaneously detecting target microorganisms in a biological sample and determining susceptibility of the microorganisms to antimicrobial agents using a nonspecific medium and a medium specific for urinary gram negative pathogens, as set forth above. JOHNSON in view of LIBMAN and THALLER do not specifically teach amoxicillin, clavulanic acid/amoxicillin, or enrofloxacin.

BROCCO teaches a method of determining susceptibility of uropathogens, to amoxicillin and a clavulanic acid mixture (p. 5, line 8-p. 6, line 7 and p. 9, line 4-p. 10, line 15).

It would have been obvious at the time of invention to include the amoxicillin and clavulanic acid of BROCCO as antimicrobial agents in the method of JOHNSON in view of LIBMAN and THALLER where the motivation would have been to test susceptibility of microorganisms, specifically urinary pathogens, to any known antibiotic or mixture of antibiotics, as suggested by JOHNSON, in order to determine an appropriate course of treatment for a subject infected with the microorganisms.

Conclusion

Claims 20-24, 26, and 31 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to a patent analyst, Tina Plunkett, whose telephone number is (703) 305-3524.

Marjorie A. Moran
Examiner
Art Unit 1631

March 25, 2002